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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,734	01/25/2002	A. Robert Spitzer	0594.00034	9911

48924 7590 10/02/2006

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EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,734	SPITZER, A. ROBERT	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,25 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *1-21,28,29,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,25 and 30* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/21/06 has been entered.

Claim Status

2. Claims 23, 24, 26 and 27 have been cancelled;

Claims 1-22, 25, and 28-32 are currently pending;

Claims 1-21, 28, 29, 31 and 32 have been withdrawn;

Claims 22, 25 and 30 are being examined in this application.

Election/Restrictions

3. Applicant elected without traverse to prosecute the invention of group II, claims 22, 25, 27, and 30, as acknowledged in the previous Office action mailed 4/11/05 at p. 3, para 6.

Priority

4. This application claims benefit of provisional application 60/264,413 filed on 01/26/2001, and provisional application 60/302,799 filed on 7/3/2001.

Claim Rejections Withdrawn

5. Upon further consideration and in light of applicant's amendments to the claims, the following rejections are withdrawn:

A.) Claims 22, 25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,500,221 (Murata et al).

B.) Claims 22, 25, 27, and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,268,396 (B1) (Nau et al).

C.) Claims 22, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 4,369,172 (Schor et al).

Discussion and Answer to Argument

6. Applicants' traversal over the above listed rejections is moot, because the claim rejections are withdrawn.

New Claim Objections/Rejections

Claim Objections

7. Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 recites a medicine suppository consisting "an effective amount of appropriate medication for the effective treatment of a migraine headache". The phrase "appropriate medication" can be interpreted to mean that the "said medication" is any

medication and not just limited to the medications (including valproate, sodium valproate, and valproate) recited in the independent Claim 22. In other words, the instant Claim 25 broadens the scope for the claimed "medication".

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

9. Claims 22 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "a medicine suppository consisting of an effective amount of a medication selected from the group consisting of valproate, sodium valproate, and valproate salts for the treatment of a migraine headache in a suppository".

The transitional phrase "consisting of" is a closed term, and excludes all other elements not specified in the claim. See MPEP 2111.03.

> The transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("consisting of" defined as "closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.").

The instant claim (Claim 22) is, therefore, interpreted to mean a "suppository" consisting of only the medication (selected from valproate, sodium valproate, or valproate salts), and nothing else.

However, the instant specification does not disclose "a suppository" that "consist of" only valproate, sodium valproate, or valproate salts. The instant specification discloses "medication composition" that "includes" various chemical compounds such as the ones listed at p. 5, lines 12+. The instant specification also discloses that the "medication composition" would comprise other ingredients so that the medication composition can be in various forms such as liquid, gel, paste, suspension, etc., as disclosed at p. 5, lines 22. The instant specification also discloses that the medication composition can include other substances such as thickeners, pharmaceutical carriers, solvents, etc. More specifically, the instant specification discloses that "the suppository" includes other ingredients such as various carriers at p. 13, lines 7+. That is the instant specification does not show possession of "a medicine suppository" that only consisting of sodium valproate, valproate salts or valproate for the treatment of a migraine headache.

Scope of Enablement Rejection

10. Claims 22, 25 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and/or using a suppository composition comprising valproate, valproate salts, or sodium valproate, and other pharmaceutical carriers, does not reasonably provide enablement for making and/or using a suppository consisting of only valproate, valproate salts, or sodium valproate. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims/The nature of the invention

The breadth of the instant Claim 22 seems to encompass a medicine suppository that consists of only valproate, valproate salts, or sodium valproate. The instant Claims 25 and 30 encompass medicine suppositories that comprise valproate, valproate salts, or sodium valproate and other ingredients as part of the suppositories. The instant claims 25 and 30 can also be interpreted to mean that the claimed medicine suppositories consist of only valproate, valproate salts, or sodium valproate with no other ingredients as part of the suppositories.

The state of the prior art/ The predictablility or lack thereof in the art

The term "suppository" as defined in the art is to mean a composition comprising not only the active chemical ingredient, but also suppository bases that are part of the required formulation. See definition for the term "suppository" in Stedman's Medical Dictionary (27th Edition; 2000). The state of the prior art teaches that suppositories are comprised not only of the active chemical compound (such valproate), but also the necessary suppository bases and other pharmaceutical ingredients as parts of the overall suppository formulation.

For examples, Murata et al (US 5,500,221; 3/19/1996; cited in the previous Office action, mailed 2/21/06), throughout the patent, teaches formulation of suppositories comprising acidic drugs such as sodium valproate (cols. 1-2, especially, lines 25+). Murata et al teach base components are commonly used for suppositories (col. 2, lines 50+), and additional acidic compounds that are capable of acidifying the site where the suppository is administered is also needed as part of the suppository composition (col. 2, lines 34+).

Van Hoogdalem et al (Clin. Pharmacokinet. Vol. 21 (1): 11-26; 1991), throughout the reference, reviews rectal drug administration of various drug formulations such as valproate suppository (Summary and p. 19-20). Van Hoogdalem et al, teach suppository bases in addition to drug substances are part of a suppository (p. 14, left col., para 2). The reference also teaches the problem of proper release of the drug substance from the suppository and the need for the drug substance to be dissolved into the rectal fluid for absorption (p. 14, left col., para 2). In addition, the reference also teaches various problems with rectal administration of different drugs such as rectal irritation and induction of rectal ulceration in humans (p. 16-17). The reference

also teaches that certain drug substances can cause local irritation and may compromise mucosal integrity (p. 17, left col., para 1).

Valproic acid is an acid (see "Valproic Acid", Merck Index. 13th edition. 2001), and thus would at least cause local irritation if administer by itself without any other suppository bases or pharmaceutical ingredients. As summarized in the Merck Index, valproic acid (or valproate) is a colorless liquid, which is not a solid as defined by the term "suppository". Without appropriate formulation that comprises other ingredients, valproic acid cannot be made into a suppository that is a solid. In addition, administering the pure Valproic acid compound in its liquid form would have problems such as leakage from the orifice where the drug was administered, which problem is discussed in the instant specification at p. 6, lines 20+. Furthermore, valproic acid has different solubility in different solutions as indicated in the Merck Index. Without formulations with additional ingredients, the compound might not dissolve in the rectal fluid, and thus prevent absorption into the blood.

The sodium salt of the valproate (sodium valproate) is a solid in the form of deliquescent powder as specified by the Merck Index. Without addition of any formulation ingredients, the compound sodium valproate would be in a powder form, and thus the success of rectal administering would be questionable. The compound also has different solubility in different solutions as stated in the Merck Index, and thus presents problems for absorption by the rectal tissue.

Therefore, the success of making a suppository composition consisting only of the pure active chemical compound (i.e. valproate, sodium valproate, or valproate salts) is highly

unpredictable. Furthermore, administering the pure compounds either in the liquid form or the solid powder form would cause undesirable effects, and would have questionable success rate.

The level of one of ordinary skill

The level of skill is high and requires PhD/MD.

The amount of direction or guidance present/The presence or absence of working examples

The only guidance present in the instant specification is directed to suppository composition that comprises the specific chemical active ingredients (i.e. valproate) and other pharmaceutical carriers (e.g. pp. 12-13). There is no guidance described for making a suppository consisting of only valproate or its salts. The specification does not provide any experimental and/or clinical data indicating the success of making a suppository consisting of only valproate and its successful administration to patients for treating migraine.

The quantity of experimentation needed

Due to the unpredictabilities of making suppositories with pure chemical compounds such as problems with general formulation, local irritation, leakage, solubility, and availability for absorption, undue experimentation would be required. As discussed above, the art only generally demonstrates medicine suppository that is formulated into a solid composition comprising both active drug compounds and other pharmaceutical ingredients that are necessary for successful formulation and administration. The art also demonstrates various problems with

rectal administering for different drugs, as discussed above. Thus, undue experimentation would be required to make and use the instant claimed composition.

Conclusion

Due to the non-routine experimentation necessary to determine the specific formulation of the claimed suppository and the success of making valproate (valproic acid or sodium valproate) into a medicine suppository; the lack of direction/guidance presented in the specification regarding the specific requirements for the claimed product; the unpredictability of the making and/or using a suppository consisting only of the active drug ingredient as established by the state of the prior art; the breadth of the claims, undue experimentation would be required of a skilled artisan to make and/or use the claimed invention in its full scope.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 22, 25 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites the limitation "the treatment of a migraine" in line 3 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 25 recites the limitation "the effective treatment of a migraine" in lines 2-3 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 30 recites the limitation "the rectum of an individual" in line 4 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 22 recites the term "suppository", which is unclear and confusing. The instant specification discloses "suppository" to be in different forms and comprises various medications, and the "main medications" used in the suppository is valproate and other valproate derivatives and/or salts (p. 12, lines 28+). The instant specification also discloses that the "suppository further includes other ingredients including, but not limited to, various carriers and substances including, but not limited to, glycerin and sodium stearate" at p. 13, lines 7+. Thus, it is reasonable for a person of ordinary skill in the art to conclude that a "suppository" as defined and used in the instant application does not only comprise the "medication", but also requires other ingredients. In addition, the term "suppository" is known in the art to mean a solid body shaped for introducing into one of the orifices (e.g. rectum, urethra, vagina) of the body other than the oral cavity, and is comprised of medication and suppository bases. See definition for the term "suppository" in Stedman's Medical Dictionary (27th Edition; 2000).

However, the instant Claim 22 recites that "a medicine suppository consisting of an effective amount of a medication..." The transitional phrase "consisting of" is a closed term, and excludes all other elements as discussed above. See MPEP 2111.03. The instant claim (Claim 22) is interpreted to mean a "suppository" consisting of only the medication (selected from valproate, sodium valproate, or valproate salts), but nothing else. This is in direct conflict with the definition for the term "suppository" used in the instant specification and in the art. Thus, one of ordinary skill in the art would not be able to clearly define the metes and bounds of the claimed product ("a suppository").

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

14. Claims 22 and 25 are rejected under **35 U.S.C. 102(b)** as being anticipated by Bauer et al (US 4,558,070; 12/10/1985).

The instant claims recite a medicine suppository consisting of an effective amount of a medication selected from the group consisting of valproate, sodium valporate, and valporate slats for the treatment of a migraine headache in a suppository. As discussed above in the rejection under the second paragraph of 35 U.S.C. 112, the claim language is unclear. The claim can be interpreted to drawn on a composition consists of only valporate, sodium valporate or valproate salts. The recitation of "for the treatment of a migraine headache" is construed as intended use of the claimed composition.

Bauer et al, throughout the patent, teach compositions that consists of valproic acid (or valproate), or sodium valporate (see col. 1, especially lines 20+), which reads on the claimed compositions of valporate, sodium valproate or valproate salts as recited in **clms 22** and **25.**

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over van Hoogdalem et al (Clin. Pharmacokinet. Vol. 21 (1): 11-26; 1991), in view of Raskin (The Western Journal of Medicine. Vol. 161: 299-302; 1994).

The instant claim recites a method of treating a migraine headache consisting of the step of administering an effective amount of a medication selected from the group consisting of valproate, sodium valproate, and valproate salts in a suppository into the rectum of an individual.

Van Hoogdalem et al, throughout the reference, teach rectal drug administration of various drug formulations such as valproate suppository (Summary and p. 19-20). The reference teaches using valproic acid or sodium valporate formulated as suppository for treatment of epilepsy (pp. 19-20), which reads on the method consisting of the step of administering an effective amount of a medication (valproate, sodium valproate or valproate salts) in a suppository into the rectum of an individual because by definition suppository is administered through the rectum (see "suppository" in Stedman's Medical Dictionary 27th edition).

Van Hoogdalem et al do not specifically teach using the valproate suppository to treat migraine.

However, Raskin teaches using valporate sodium for treatment of migraine (see Table 1 of the reference). The reference also teaches valporate sodium "appears to be remarkably effective" in treating migraine (p. 302, para 3).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to using valproate in the form of a suppository to treat migraine.

A person of ordinary skill in the art would have been motivated at the time of the invention to use valporate in the form of a suppository to treat migraine, because valproate, sodium valproate or valproate salts is shown to be effective in treating migraine.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications because valporate has been successfully formulated into and administered as suppositories as taught by van Hoogdalem et al, and valproate has also been shown to effectively treat migraine.

17. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen (Acta Neurologica Scandinavica. Vol. 78: 346-348; 1988), in view of Murata (US 5,500,221; 3/19/1996; cited in the previous Office action, mailed 2/21/06).

Sorensen, throughout the reference, teaches using valporate to treat migraine (see Abstract of the reference).

Sorensen does not specifically teach the valproate or its salts is administered as a suppository.

However, Murata et al, throughout the reference, teaches formulation of valporate and its salts (sodium valproate) into a suppository (see Claim 1 of the reference). The reference also

teaches the advantages of formulating drugs into suppositories such as avoiding decomposition of drugs by acid or enzyme in gastrointestinal tract, and safer and easier to administer than injection (col. 1, lines 15+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to using valproate in the form of a suppository to treat migraine.

A person of ordinary skill in the art would have been motivated at the time of the invention to use valporate in the form of a suppository to treat migraine, because suppository has a number of advantages such as less decomposition, and safer and easier administering than injection as discussed above.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications because valporate or its salts (such as sodium valporate) has been successfully formulated into suppositories as taught by Murata et al, and valproate has also been shown to effectively treat migraine as taught by Sorensen.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached at 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
9/21/2006

MARK SHIBUYA, PH.D.
PATENT EXAMINER